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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/768,185	01/24/2001	Francis Kalush	CL000280	1938

25748 7590 01/13/2004

CELERA GENOMICS CORP.
ATTN: WAYNE MONTGOMERY, VICE PRES, INTEL PROPERTY
45 WEST GUDE DRIVE
C2-4#20
ROCKVILLE, MD 20850

EXAMINER	
MURPHY, JOSEPH F	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 01/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/768,185	KALUSH ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-26 and 28-40* is/are pending in the application.

4a) Of the above claim(s) *22-25,28-31 and 33-36* is/are withdrawn from consideration.

5)☒ Claim(s) *20,26,32 and 39* is/are allowed.

6)☒ Claim(s) *18,19,21,37,38 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Formal Matters

Claims 18-26, 28-40 are pending. Claims 22-25, 28-31, 33-36 stand withdrawn from consideration pursuant to 37 CFR 1.142(b). Claims 18-21, 26, 32, 37-40 are under consideration.

Response to Amendment

Applicant's amendment and arguments filed 10/28/2003 have been fully considered but they are not persuasive, for the reasons set forth below.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-19, 21, 37-38, 40 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid sequence of SEQ ID NO: 1, wherein the nucleotide at position 89837 is 'T' instead of 'C', does not reasonably provide enablement for a nucleic acid sequence which comprises at least 20 or 30 contiguous nucleotides of SEQ ID NO: 1, with the T to C mutation, and a nucleic acid sequence which comprises nucleotides from 89803-89998 of SEQ ID NO: 1, with the T to C mutation, for reasons of record set forth in the Office Action of 7/28/2003. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection of record set forth that the claims encompass a nucleic acid sequence which comprises at least 20 or 30 contiguous nucleotides of SEQ ID NO: 1, with the T to C mutation, and a nucleic acid sequence which comprises nucleotides from 89803-89998 of SEQ ID NO: 1, with the T to C mutation. The specification discloses that SEQ ID NO: 1 encodes an estrogen receptor. The art teaches that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. For example, Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph). Since the claims encompass variant nucleic acids and given the art recognized unpredictability of the effect of mutations on protein function, it would require undue experimentation to make and use the claimed invention. The Voet reference demonstrates that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. Working examples are provided for SEQ ID NO: 1 encoding estrogen receptor beta. Given the breadth of claims 18-19, 21, 37-38, 40 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

The claims do not include a functional limitation for the claimed nucleic acids. Since detailed information regarding the structural and functional requirements of the nucleic acids encoding polypeptides are lacking, it is unpredictable as to which encoding variations, if any, meet the limitations of the claims. Furthermore, since the claims are drawn to a nucleic acid sequence which comprises at least 20 or 30 contiguous nucleotides of SEQ ID NO: 1, with the T to C mutation, and a nucleic acid sequence which comprises nucleotides from 89803-89998 of SEQ ID NO: 1, with the T to C mutation, while the claims do not recite a functional limitation for the encompassed nucleic acids encoding amino acid sequences, there is not sufficient direction as to how to use the encompassed nucleic acids encoding polypeptides which do not function as an estrogen receptor. Since no functional language is associated with the claims one of ordinary skill in the art would not know how to use these defined sequences except in further characterization of the sequences themselves.

Applicant has amended the claims by adding the limitation wherein the nucleic acid encodes an estrogen receptor beta peptide, and argues that this is a function that the encoded polypeptide must have and that therefore the claims meet the enablement requirement. However, the claims as amended do not set forth a functional limitation for the encoded polypeptide. The fact that the encoded peptide is an estrogen receptor beta peptide does not mean that the encoded peptide must retain any particular function.

Since these peptides do not need to have any particular function, it would require undue experimentation for one of skill in the art to make and use the claimed nucleic acids, since the skilled artisan would have to first make nucleic acid sequence which comprises at least 20 or 30 contiguous nucleotides of SEQ ID NO: 1, with the T to C mutation, and a nucleic acid sequence

which comprises nucleotides from 89803-89998 of SEQ ID NO: 1, with the T to C mutation, and then determine whether the encoded peptides had any particular function. Applicant is required to enable one of skill in the art to make and use the claimed invention, while the claims encompass polynucleotides encoding peptides for which the skilled artisan would have to test for function. Since the claims do not enable one of skill in the art to make and use peptide fragments, and since detailed information regarding the structural and functional requirements of the peptides are lacking, it is unpredictable as to which peptides, if any, meet the limitations of the claims.

Claims 18-19, 21, 37-38, 40 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record set forth in the Office Action of 7/28/2003. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The rejection of record set forth that these are genus claims. The claims are drawn to a nucleic acid sequence which comprises at least 20 or 30 contiguous nucleotides of SEQ ID NO: 1, with the T to C mutation, and a nucleic acid sequence which comprises nucleotides from 89803-89998 of SEQ ID NO: 1, with the T to C mutation. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to describe more than a single species of the genus, the claims do not include a functional limitation for the claimed nucleic acids, and because one of skill in the art could not be expected to predict the biological activity of the sequence variants encompassed by the claims, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of polynucleotides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from other seven transmembrane region compounds are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides encompassed: there is no guidance in the

art as to what the defining characteristics of the peptides might be. Thus, applicant was not in possession of the claimed genus.

Applicant has amended the claims by adding the limitation wherein the nucleic acid encodes an estrogen receptor beta peptide, and argues that this is a function that the encoded polypeptide must have and that therefore the claims meet the written description requirement. However, the claims as amended do not set forth a functional limitation for the encoded polypeptide. The fact that the encoded peptide is an estrogen receptor beta peptide does not mean that the encoded peptide must retain any particular function. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, no function is set forth for the encoded peptides, and There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from other seven transmembrane region compounds are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polypeptides encompassed: there is no guidance in the art as to what the defining characteristics of the polypeptides might

be. Thus, no identifying characteristics or properties of the instant polynucleotides encoding polypeptides are provided such that one of skill would be able to predictably identify the molecules that would be peptides of an estrogen receptor beta peptide.

Conclusion

Claims 20, 26, 32, 39 are allowable.

Claims 18-19, 21, 37-38, 40 are rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
December 31, 2003

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600